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NEWS 27 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985
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NEWS 29 Oct 24 BEILSTEIN adds new search fields
NEWS 30 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 31 Oct 25 MEDLINE SDI run of October 8, 2002
NEWS 32 Nov 18 DKILIT has been renamed APOLLIT
NEWS 33 Nov 25 More calculated properties added to REGISTRY
NEWS 34 Dec 02 TIBKAT will be removed from STN
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or Bonnerot C?/au
L1 616 BENAROCH P?/AU OR VINCENT-SCHNEIDER H?/AU OR STUMPTER P?/AU OR
AMIGORENA S?/AU OR BONNEROT C?/AU

=> s l1 and vesicle?
L2 75 L1 AND VESICLE?

=> s 12 and mastocyst?
L3 0 L2 AND MASTOCYST?

=> s 12 and mastocyte?
L4 0 L2 AND MASTOCYTE?

=> s 11 and mastocyte
L5 0 L1 AND MASTOCYTE

=> s 12 and exosome?
L6 38 L2 AND EXOSOME?

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L7 O L6 AND BASOPHIL?

=> dup rem 16
PROCESSING COMPLETED FOR L6
L8 16 DUP REM L6 (22 DUPLICATES REMOVED)

=> dis 18 1-16 ibib abs

L8 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:894235 CAPLUS
TITLE: Indirect activation of naive CD4+ T cells by dendritic cell-derived **exosomes**
AUTHOR(S): Thery, Clotilde; Duban, Livine; Segura, Elodie; Veron, Philippe; Lantz, Olivier; Amigorena, Sebastian
CORPORATE SOURCE: INSERM U520, Institut Curie, 12 rue Lhomond, Paris, 75005, Fr.
SOURCE: Nature Immunology (2002), 3(12), 1156-1162
CODEN: NIAMCZ; ISSN: 1529-2908
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Dendritic cells (DCs) secrete **vesicles** of endosomal origin, called **exosomes**, that bear major histocompatibility complex (MHC) and T cell costimulatory mols. Here, we found that injection of antigen- or peptide-bearing **exosomes** induced antigen-specific naive CD4+ T cell activation in vivo. In vitro, **exosomes** did not induce antigen-dependent T cell stimulation unless mature CD8.alpha.- DCs were also present in the cultures. These mature DCs could be MHC class II-neg., but had to bear CD80 and CD86. Therefore, in addn. to carrying antigen, **exosomes** promote the exchange of functional peptide-MHC complexes between DCs. Such a mechanism may increase the no. of DCs bearing a particular peptide, thus amplifying the initiation of primary adaptive immune responses.

L8 ANSWER 2 OF 16 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002352649 IN-PROCESS
DOCUMENT NUMBER: 22090603 PubMed ID: 12096030
TITLE: **Exosomes** bearing HLA-DR1 molecules need dendritic cells to efficiently stimulate specific T cells.
AUTHOR: Vincent-Schneider Helene; Stumptner-Cuvelette Pamela; Lankar Danielle; Pain Sabine; Raposo Graca; Benaroch Philippe; Bonnerot Christian
CORPORATE SOURCE: INSERM U520, Institut Curie, 26 rue d'Ulm, 75248 Paris Cedex 05, France. CNRS, UMR 144, Institut Curie, 12 rue Lhomond, 75005 Paris, France.
SOURCE: INTERNATIONAL IMMUNOLOGY, (2002 Jul) 14 (7) 713-22.
Journal code: 8916182. ISSN: 0953-8178.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20020704
Last Updated on STN: 20020704

AB **Exosomes** are small **vesicles** (60-100 nm) secreted by various cell types upon the fusion of endosomal compartments with the plasma membrane. **Exosomes** from antigen-presenting cells (APC), such as B lymphocytes and dendritic cells (DC), bear MHC class II molecules. In addition, the injection of DC-derived **exosomes** was reported to elicit potent T cell responses in vivo. Here, we analyzed the activation of specific T cells by MHC class II-bearing **exosomes** in vitro. The rat mast cell line, RBL-2H3, was engineered to express human class II molecules uniformly loaded with an antigenic peptide [HLA-DR1-hemagglutinin (HA)]. These cells secreted **exosomes** bearing DR1 class II molecules upon stimulation by a calcium ionophore or IgE receptor cross-linking. **Exosomes** bearing DR1-HA(306-318) complexes activated HA/DR1-specific T cells only weakly, whereas the

cross-linking of such **exosomes** to latex beads increased stimulation of specific T cells. By contrast, the incubation of free **exosomes** with DC resulted in the highly efficient stimulation of specific T cells. Thus, **exosomes** bearing MHC class II complexes must be taken up by professional APC for efficient T cell activation.

L8 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:575897 CAPLUS
DOCUMENT NUMBER: 137:183978
TITLE: **Exosomes**: Composition, Biogenesis and Function
AUTHOR(S): Thery, Clotilde; Zitvogel, Laurence; Amigorena, Sebastian
CORPORATE SOURCE: INSERM U520, Institut Curie, Paris, 75005, Fr.
SOURCE: Nature Reviews Immunology (2002), 2(8), 569-579
CODEN: NRIABX; ISSN: 1474-1733
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. **Exosomes** are small membrane **vesicles** of endocytic origin that are secreted by most cells in culture. Interest in **exosomes** has intensified after their recent description in antigen-presenting cells and the observation that they can stimulate immune responses *in vivo*. In the past few years, several groups have reported the secretion of **exosomes** by various cell types, and have discussed their potential biol. functions. Here, we describe the phys. properties that define **exosomes** as a specific population of secreted **vesicles**, we summarize their biol. effects, particularly on the immune system, and we discuss the potential roles that secreted **vesicles** could have as intercellular messengers.
REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 16 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002398522 MEDLINE
DOCUMENT NUMBER: 22142699 PubMed ID: 12147373
TITLE: Malignant effusions and immunogenic tumour-derived **exosomes**.
COMMENT: Comment in: Lancet. 2002 Jul 27;360(9329):268
AUTHOR: Andre Fabrice; Schartz Noel E C; Movassagh Mojgan; Flament Caroline; Pautier Patricia; Morice Philippe; Pomeil Christophe; Lhomme Catherine; Escudier Bernard; Le Chevalier Thierry; Tursz Thomas; Amigorena Sebastian; Raposo Graca; Angevin Eric; Zitvogel Laurence
CORPORATE SOURCE: Departments of Clinical Biology, Immunology Unit, Institut Gustave Roussy, Villejuif, France.
SOURCE: LANCET, (2002 Jul 27) 360 (9329) 295-305.
Journal code: 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020731
Last Updated on STN: 20020810
Entered Medline: 20020809

AB BACKGROUND: **Exosomes** derived from tumours are small **vesicles** released *in vitro* by tumour cell lines in culture supernatants. To assess the role of these **exosomes** *in vivo*, we examined malignant effusions for their presence. We also investigated whether these **exosomes** could induce production of tumour-specific T cells when pulsed with dendritic cells. METHODS: We isolated **exosomes** by ultracentrifugation on sucrose and D(2)O gradients of 11 malignant effusions. We characterised **exosomes**

with Western blot analyses, immunoelectron microscopy, and in-vitro stimulations of autologous T lymphocytes. FINDINGS: Malignant effusions accumulate high numbers of membrane vesicles that have a mean diameter of 80 nm (SD 30). These vesicles have antigen-presenting molecules (MHC class-I heat-shock proteins), tetraspanins (CD81), and tumour antigens (Her2/Neu, Mart1, TRP, gp100). These criteria, including their morphological characteristics, indicate the similarities between these vesicles and exosomes.

Exosomes from patients with melanoma deliver Mart1 tumour antigens to dendritic cells derived from monocytes (MD-DCs) for cross presentation to clones of cytotoxic T lymphocytes specific to Mart1. In seven of nine patients with cancer, lymphocytes specific to the tumour could be efficiently expanded from peripheral blood cells by pulsing autologous MD-DCs with autologous ascitis exosomes. In one patient tested, we successfully expanded a restricted T-cell repertoire, which could not be recovered carcinomatosis nodules. INTERPRETATION: Exosomes derived from tumours accumulate in ascites from patients with cancer. Ascitis exosomes are a natural and new source of tumour-rejection antigens, opening up new avenues for immunisation against cancers.

L8 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:930989 CAPLUS
TITLE: Tumor-derived exosomes: a new source of tumor rejection antigens
AUTHOR(S): Andre, F.; Schartz, N. E. C.; Chaput, N.; Flament, C.; Raposo, G.; Amigorena, S.; Angevin, E.; Zitvogel, L.
CORPORATE SOURCE: Immunology Unit, Unite d'immunologie, Institut Gustave Roussy, 39 rue Camille-Desmoulins, Cedex, Villejuif, F-94805, Fr.
SOURCE: Vaccine (2002), 20(Supplement4), A28-A31
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Exosomes are small vesicles released by a broad array of hematopoietic cells. Previous studies showed that exosomes released by antigen loaded dendritic cells induce immune-mediated anti-tumor response in mice. Here, we will describe the biochemical properties of tumor-derived exosomes and, their pre-clinical activity as cancer vaccines.

L8 ANSWER 6 OF 16 MEDLINE

DUPLICATE 3

ACCESSION NUMBER: 2001333530 MEDLINE
DOCUMENT NUMBER: 21286480 PubMed ID: 11390481
TITLE: Proteomic analysis of dendritic cell-derived exosomes: a secreted subcellular compartment distinct from apoptotic vesicles.
AUTHOR: Thery C; Boussac M; Veron P; Ricciardi-Castagnoli P; Raposo G; Garin J; Amigorena S
CORPORATE SOURCE: Institut National de la Sante et de la Recherche Medical, Unite 520, Institut Curie, Paris, France..
clotilde.thery@curie.fr
SOURCE: JOURNAL OF IMMUNOLOGY, (2001 Jun 15) 166 (12) 7309-18.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010827
Last Updated on STN: 20010827
Entered Medline: 20010823
AB Dendritic cells constitutively secrete a population of small (50-90 nm

diameter) Ag-presenting vesicles called **exosomes**. When sensitized with tumor antigenic peptides, dendritic cells produce **exosomes**, which stimulate anti-tumor immune responses and the rejection of established tumors in mice. Using a systematic proteomic approach, we establish the first extensive protein map of a particular **exosome** population; 21 new exosomal proteins were thus identified. Most proteins present in **exosomes** are related to endocytic compartments. New exosomal residents include cytosolic proteins most likely involved in **exosome** biogenesis and function, mainly cytoskeleton-related (cofilin, profilin I, and elongation factor 1alpha) and intracellular membrane transport and signaling factors (such as several annexins, rab 7 and 11, rap1B, and syntenin). Importantly, we also identified a novel category of exosomal proteins related to apoptosis: thioredoxin peroxidase II, Alix, 14-3-3, and galectin-3. These findings led us to analyze possible structural relationships between **exosomes** and microvesicles released by apoptotic cells. We show that although they both represent secreted populations of membrane **vesicles** relevant to immune responses, **exosomes** and apoptotic **vesicles** are biochemically and morphologically distinct. Therefore, in addition to cytokines, dendritic cells produce a specific population of membrane **vesicles**, **exosomes**, with unique molecular composition and strong immunostimulating properties.

L8 ANSWER 7 OF 16 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002046100 EMBASE
TITLE: **Exosomes** in cancer immunotherapy: Preclinical data.
AUTHOR: Andre F.; Andersen M.; Wolfers J.; Lozier A.; Raposo G.; Serra V.; Ruegg C.; Flament C.; Angevin E.; **Amigorena S.**; Zitvogel L.
CORPORATE SOURCE: F. Andre, Immunology Unit, Institut Gustave Roussy, Villejuif, France
SOURCE: Advances in Experimental Medicine and Biology, (2001) 495/- (349-354).
Refs: 13
ISSN: 0065-2598 CODEN: AEMBAP
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
LANGUAGE: English

L8 ANSWER 8 OF 16 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001198773 MEDLINE
DOCUMENT NUMBER: 21154956 PubMed ID: 11231627
TITLE: Tumor-derived **exosomes** are a source of shared tumor rejection antigens for CTL cross-priming.
AUTHOR: Wolfers J; Lozier A; Raposo G; Regnault A; Thery C; Masurier C; Flament C; Pouzieux S; Faure F; Tursz T; Angevin E; **Amigorena S**; Zitvogel L
CORPORATE SOURCE: Immunology Unit, Department of Clinical Biology, Institut Gustave Roussy, Villejuif, France.
SOURCE: NATURE MEDICINE, (2001 Mar) 7 (3) 297-303.
Journal code: 9502015. ISSN: 1078-8956.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010410
Last Updated on STN: 20010410
Entered Medline: 20010405

AB The initiation of T-cell-mediated antitumor immune responses requires the uptake and processing of tumor antigens by dendritic cells and their presentation on MHC-I molecules. Here we show in a human in vitro model

system that **exosomes**, a population of small membrane **vesicles** secreted by living tumor cells, contain and transfer tumor antigens to dendritic cells. After mouse tumor **exosome** uptake, dendritic cells induce potent CD8+ T-cell-dependent antitumor effects on syngeneic and allogeneic established mouse tumors. Therefore, **exosomes** represent a novel source of tumor-rejection antigens for T-cell cross priming, relevant for immunointerventions.

L8 ANSWER 9 OF 16 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2001488294 MEDLINE
DOCUMENT NUMBER: 21422224 PubMed ID: 11530496
TITLE: [Exosomes derived from dendritic cells].
Les **exosomes** derives des cellules dendritiques.
AUTHOR: Amigorena S
CORPORATE SOURCE: Unite INSERM U520, Institut Curie, 12, rue Lhomond, 75005 Paris, France.
SOURCE: JOURNAL DE LA SOCIETE DE BIOLOGIE, (2001) 195 (1) 25-7.
Ref: 11
Journal code: 100890617.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20010904
Last Updated on STN: 20011029
Entered Medline: 20011025
AB Dendritic cells (DC) are potent antigen presenting cells and the only ones capable of inducing primary cytotoxic immune responses both in vivo and vitro. DCs secrete a 60-80 nm membrane **vesicle** population of endocytic origin, called **exosomes**. The protein composition of **exosomes** was analyzed using a systematic proteomic approach. Besides MHC and costimulatory molecules, **exosomes** bear several adhesion proteins, probably involved in their specific targeting. **Exosomes** also accumulate several cytosolic factors, most likely involved in exosome's biogenesis in late endosomes. Like DCs, **exosomes** induce potent anti tumor immune responses in vivo. Indeed, a single injection of DC-derived **exosomes** sensitized with tumor peptides induced the eradication of established mouse tumors. Tumor-specific cytotoxic T lymphocytes were found in the spleen of **exosome** treated mice, and depletion of CD8+ T cells in vivo inhibited the anti tumor effect of **exosomes**. These results strongly support the implementation of human DC-derived **exosomes** for cancer immunotherapy.

L8 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:335525 CAPLUS
DOCUMENT NUMBER: 132:333388
TITLE: **Exosomes** containing major histocompatibility antigens and their preparation and diagnostic and therapeutic use
INVENTOR(S): Benaroch, Philippe; Vincent-Schneider, Helene; Stumptner, Pamela; Amigorena, Sebastian; Bonnerot, Christian; Raposo, Graca
PATENT ASSIGNEE(S): Institut National de la Sante et de la Recherche Medicale, Fr.; Institut Curie; Centre National de la Recherche Scientifique
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 20000028001	A1	20000518	WO 1999-FR2691	19991104
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2785543	A1	20000512	FR 1998-13946	19981105
EP 1127110	A1	20010829	EP 1999-954055	19991104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002529074	T2	20020910	JP 2000-581168	19991104
PRIORITY APPLN. INFO.: FR 1998-13946 A 19981105				
WO 1999-FR2691 W 19991104				

AB Membrane vesicles contg. defined members of the major histocompatibility complex, and their prepn. and use as immunogens or for diagnostic and therapeutic purposes are described. The **exosomes** may carry the antigen and another mol. of interest, e.g. as a reporter or an effector. The invention also concerns methods for producing said vesicles, genetic constructs, cells and compns., useful for implementing said methods. The **exosomes** are manufd. using host cells that do not synthesize their own MHC antigens. Expression of genes for the .alpha., .beta., and const. chains of HLA-DR1 in RBL-2H3 cells led to the accumulation of the antigen in **exosomes**. The **exosomes** could be released from the cells by treatment with ionomycin. Rats inoculated with these **exosomes** raised antibodies to the antigen.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 16	MEDLINE	DUPLICATE 6
ACCESSION NUMBER: 2001098651	MEDLINE	
DOCUMENT NUMBER: 21030341	PubMed ID: 11188932	
TITLE: Cancer immunotherapy using dendritic cell-derived exosomes .		
AUTHOR: Amigorena S		
CORPORATE SOURCE: Unite INSERM U520, Institut Curie, Paris, France..		
SOURCE: sebastian.amigorena@curie.fr		
PUB. COUNTRY: Argentina		
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)		
LANGUAGE: English		
FILE SEGMENT: Priority Journals		
ENTRY MONTH: 200102		
ENTRY DATE: Entered STN: 20010322		
	Last Updated on STN: 20010322	
	Entered Medline: 20010201	

AB Dendritic cells (DCs) are the most potent antigen presenting cells and the only ones capable of inducing primary cytotoxic immune responses. We found that DCs secrete a population of membrane vesicles, called **exosomes**. **Exosomes** are 60-80 nm vesicles of endocytic origin. The protein composition of **exosomes** was subjected to a systematic proteomic analysis. Besides MHC and co-stimulatory molecules, **exosomes** bear several adhesion proteins, most likely involved in their specific subjected to targeting. We also found that **exosomes** accumulate several cytosolic factors, probably involved in their endosomal biogenesis. Like DCs,

exosomes induced immune responses *in vivo*. Indeed, a single injection of DC-derived **exosomes** sensitized with tumor peptides induced potent anti tumor immune responses in mice and the eradication of established tumors. Tumor-specific cytotoxic T lymphocytes were found in the spleen of **exosome**-treated mice, and the anti tumor effect of **exosomes** was sensitive to *in vivo* depletion of CD8+ T cells. These results show that **exosomes** induce potent anti tumor effects *in vivo*, and strongly support the implementation of human DC-derived **exosomes** for cancer immunotherapy.

L8 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:16570 CAPLUS
DOCUMENT NUMBER: 130:236031
TITLE: Dendritic cell-derived **exosomes**: potent immunogenic cell-free vaccines
AUTHOR(S): Zitvogel, Laurence; Regnault, Armelle; Lozier, Anne; Raposo, Graca; **Amigorena, Sebastian**
CORPORATE SOURCE: Laboratoire d'Immunologie Cellulaire, Departement de Biologie Clinique, Institut Gustave Roussy, Villejuif, Fr.
SOURCE: Dendritic Cells (1999), 643-652. Editor(s): Lotze, Michael T.; Thomson, Angus W. Academic: San Diego, Calif.
CODEN: 67DCAA
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 18 refs. discussing dendritic cell secretion of internal **vesicles** of multivesicular late endosomes, allostimulatory capacity and antigen presentation function of **exosomes**, and suppression of tumor growth by tumor peptide-pulsed dendritic cell-derived **exosomes**.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 16 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 2000014998 MEDLINE
DOCUMENT NUMBER: 20014998 PubMed ID: 10545503
TITLE: Molecular characterization of dendritic cell-derived **exosomes**. Selective accumulation of the heat shock protein hsc73.
AUTHOR: Thery C; Regnault A; Garin J; Wolfers J; Zitvogel L; Ricciardi-Castagnoli P; Raposo G; **Amigorena S**
CORPORATE SOURCE: Institut National de la Sante et de la Recherche Medicale, U520, Institut Curie, 75005 Paris, France.
SOURCE: JOURNAL OF CELL BIOLOGY, (1999 Nov 1) 147 (3) 599-610.
Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991124

AB **Exosomes** are membrane **vesicles** secreted by hematopoietic cells upon fusion of late multivesicular endosomes with the plasma membrane. Dendritic cell (DC)-derived **exosomes** induce potent antitumor immune responses in mice, resulting in the regression of established tumors (Zitvogel, L., A. Regnault, A. Lozier, J. Wolfers, C. Flament, D. Tenza, P. Ricciardi-Castagnoli, G. Raposo, and S. Amigorena. 1998. *Nat. Med.* 4:594-600). To unravel the molecular basis of **exosome**-induced immune stimulation, we now analyze the regulation of their production during DC maturation and characterize extensively their protein composition by peptide mass mapping. **Exosomes** contain several cytosolic proteins (including annexin II, heat shock

cognate protein hsc73, and heteromeric G protein Gi2alpha), as well as different integral or peripherally associated membrane proteins (major histocompatibility complex class II, Mac-1 integrin, CD9, milk fat globule-EGF-factor VIII [MFG-E8]). MFG-E8, the major exosomal component, binds integrins expressed by DCs and macrophages, suggesting that it may be involved in **exosome** targeting to these professional antigen-presenting cells. Another **exosome** component is hsc73, a cytosolic heat shock protein (hsp) also present in DC endocytic compartments. hsc73 was shown to induce antitumor immune responses *in vivo*, and therefore could be involved in the **exosome**'s potent antitumor effects. Finally, **exosome** production is downregulated upon DC maturation, indicating that *in vivo*, **exosomes** are produced by immature DCs in peripheral tissues. Thus, DC-derived **exosomes** accumulate a defined subset of cellular proteins reflecting their endosomal biogenesis and accounting for their biological function.

L8 ANSWER 14 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:173858 BIOSIS
DOCUMENT NUMBER: PREV199900173858
TITLE: Cross-presentation of tumor derived-**exosomes**: A possible mechanism for CTL-restricted antitumor immunity *in vivo*.
AUTHOR(S): Zitvogel, L.; Lozier, A.; Wolfers, J.; Regnault, A.; Raposo, G.; **Amigorena, S.**
CORPORATE SOURCE: Laboratoire d'Immunologie Clinique, Institut Gustave Roussy, Villejuif 94805 France
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1999) Vol. 40, pp. 425.
Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania, USA April 10-14, 1999 American Association for Cancer Research
. ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 15 OF 16 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 1998244633 MEDLINE
DOCUMENT NUMBER: 98244633 PubMed ID: 9585234
TITLE: Eradication of established murine tumors using a novel cell-free vaccine: dendritic cell-derived **exosomes**
AUTHOR: Zitvogel L; Regnault A; Lozier A; Wolfers J; Flament C; Tenza D; Ricciardi-Castagnoli P; Raposo G; **Amigorena S**
CORPORATE SOURCE: CNRS URA 1301, Institut Gustave Roussy, Villejuif, France.
SOURCE: NATURE MEDICINE, (1998 May) 4 (5) 594-600.
Journal code: 9502015. ISSN: 1078-8956.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980611
Last Updated on STN: 19980611
Entered Medline: 19980529

AB Dendritic cells (DCs) are professional antigen presenting cells with the unique capacity to induce primary and secondary immune responses *in vivo*. Here, we show that DCs secrete antigen presenting vesicles, called **exosomes**, which express functional Major Histocompatibility Complex class I and class II, and T-cell costimulatory molecules. Tumor peptide-pulsed DC-derived **exosomes** prime specific cytotoxic T lymphocytes *in vivo* and eradicate or suppress growth of established murine tumors in a T cell-dependent manner. **Exosome**

-based cell-free vaccines represent an alternative to DC adoptive therapy for suppressing tumor growth.

L8 ANSWER 16 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:413882 BIOSIS
DOCUMENT NUMBER: PREV199800413882
TITLE: Dendritic cell-derived **exosomes** elicit potent anti-tumor immune responses *in vivo*.
AUTHOR(S): **Amigorena, S.** (1)
CORPORATE SOURCE: (1) CJF95-01 INSERM, Inst. Curie, 12 rue Lhomond, F-75005 Paris France
SOURCE: Hematology and Cell Therapy, (April, 1998) Vol. 40, No. 2, pp. 87-89.
Meeting Info.: 8th Cell Therapy Workshop AMGEN-ROCHE Paris, France April 9, 1998
ISSN: 1269-3286.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English; French

=> dis his

(FILE 'HOME' ENTERED AT 09:53:25 ON 11 DEC 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 09:53:51 ON 11 DEC 2002
L1 616 S BENAROCH P?/AU OR VINCENT-SCHNEIDER H?/AU OR STUMPTER P?/AU O
L2 75 S L1 AND VESICLE?
L3 0 S L2 AND MASTOCYST?
L4 0 S L2 AND MASTOCYTE?
L5 0 S L1 AND MASTOCYTE
L6 38 S L2 AND EXOSOME?
L7 0 S L6 AND BASOPHIL?
L8 16 DUP REM L6 (22 DUPLICATES REMOVED)

=> s (basophil? or mast) (P) vesicle
L9 1291 (BASOPHIL? OR MAST) (P) VESICLE

=> s (basophil? or mast) (P) exosome?
L10 22 (BASOPHIL? OR MAST) (P) EXOSOME?

=> dup rem l22
L22 IS NOT VALID HERE
The L-number entered has not been defined in this session, or it has been deleted. To see the L-numbers currently defined in this session, enter DISPLAY HISTORY at an arrow prompt (=>).

=> dup rem 10
ENTER L# LIST OR (END):end

=> dup rem L10
PROCESSING COMPLETED FOR L10
L11 12 DUP REM L10 (10 DUPLICATES REMOVED)

=> dis l11 not 16
L6 IS NOT VALID HERE
For an explanation, enter "HELP DISPLAY".

=> s l11 not 16
L12 10 L11 NOT L6

=> dis l12 1-10 ibib abs

L12 ANSWER 1 OF 10 MEDLINE
ACCESSION NUMBER: 2002460092 IN-PROCESS

DOCUMENT NUMBER: 22207481 PubMed ID: 12217408
TITLE: Immunoregulatory properties of **mast** cell-derived **exosomes**.
AUTHOR: Dimitris Skokos; Hany Goubran; Michele Roa; Salah Mecheri
CORPORATE SOURCE: Unite d'Immuno-allergie, Institut Pasteur, 25 rue Dr Roux,
75724 Cedex 15, Paris, France.
SOURCE: MOLECULAR IMMUNOLOGY, (2002 Sep) 38 (16-18) 1359.
Journal code: 7905289. ISSN: 0161-5890.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20020910
Last Updated on STN: 20020910

AB Transmission of information from **mast** cells to neighboring or distant cells must be established continuously in order to ensure homeostasis or to initiate immune and inflammatory responses. Owing to their strategic location in peripheral tissues and their prompt response to various stimuli, **mast** cells can be considered as the cell prototype to fulfill such a sentinel function. There are several ways for **mast** cells to communicate with other cells including cell-cell interactions via membrane-associated receptors, cytokines and other soluble mediators, and a newly described messenger which consists of membrane vesicles called **exosomes** carrying a number of immunoregulatory molecules.

L12 ANSWER 2 OF 10 MEDLINE
ACCESSION NUMBER: 2001262354 MEDLINE
DOCUMENT NUMBER: 21203262 PubMed ID: 11306949
TITLE: Nonspecific B and T cell-stimulatory activity mediated by **mast** cells is associated with **exosomes**.
AUTHOR: Skokos D; Le Panse S; Villa I; Rousselle J C; Peronet R;
Namane A; David B; Mecheri S
CORPORATE SOURCE: Unite d'Immuno-Allergie, Institut Pasteur, Paris, France.
SOURCE: INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2001
Jan-Mar) 124 (1-3) 133-6.
Journal code: 9211652. ISSN: 1018-2438.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered Medline: 20010517

AB Bone marrow-derived mouse **mast** cells (BMMC) and **mast** cell lines P815 and MC9 have recently been shown to induce antigen-independent B and T lymphocyte activation. It has been demonstrated that a physical contact between **mast** cells and B and T lymphocytes is not necessary since **mast** cell supernatants contain full activity. Electron microscopy studies revealed the presence in **mast** cell supernatants of small vesicles called **exosomes** with a heterogeneous size from 60 to 100 nm of diameter. When cocultured with spleen cells, purified **exosomes** induce B and T cell blast formation, proliferation as well as IL-2 and IFN-gamma production. In contrast to P815 and MC9 **mast** cell lines, a pretreatment with IL-4 is required for BMMC to produce active **exosomes**. Structurally, these **exosomes** were found to harbor immunologically relevant molecules such as MHC class II, CD86, LFA-1 and ICAM-1. Here we provide for the first time the evidence that **mast** cells use **exosomes** as sophisticated messengers to communicate with cells of the immune system.

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L12 ANSWER 3 OF 10 MEDLINE

ACCESSION NUMBER: 2001139789 MEDLINE
DOCUMENT NUMBER: 20581148 PubMed ID: 11145662
TITLE: **Mast** cell-dependent B and T lymphocyte activation
is mediated by the secretion of immunologically active
exosomes.
AUTHOR: Skokos D; Le Panse S; Villa I; Rousselle J C; Peronet R;
David B; Namane A; Mecheri S
CORPORATE SOURCE: Unite d'Immuno-Allergie, Institut Pasteur, Paris, France.
Institut Jacques Monod, Unite Mixte de Recherche 7592,
Paris, France.
SOURCE: JOURNAL OF IMMUNOLOGY, (2001 Jan 15) 166 (2) 868-76.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010308

AB Mitogenic activity of bone marrow-derived mouse **mast** cells and
mast cell lines P815 and MC/9 on B and T lymphocytes is present in
their culture supernatants. To identify this activity, **mast**
cells were incubated in serum-free medium and the supernatant was
subjected to differential centrifugation, which resulted in two fractions,
the hypodense and dense fraction (pellet). When analyzed for their
mitogenic activity on spleen cells, all activity was found to be
associated with the dense fraction. Electron microscopy studies revealed
the presence in this fraction of small vesicles called **exosomes**
with a heterogeneous size from 60 to 100 nm of diameter. When cocultured
with spleen cells, purified **exosomes** induced blast formation,
proliferation, as well as IL-2 and IFN-gamma production, but no detectable
IL-4. Similar data were obtained by injecting **exosomes** into
naive mice. In contrast to **mast** cell lines, a pretreatment with
IL-4 is required for bone marrow-derived **mast** cells to secrete
active **exosomes**. Structurally, **exosomes** were found to
harbor immunologically relevant molecules such as MHC class II, CD86,
LFA-1, and ICAM-1. These findings indicate that **mast** cells can
represent a critical component of the immunoregulatory network through
secreted **exosomes** that display mitogenic activity on B and T
lymphocytes both in vitro and in vivo.

L12 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:662693 CAPLUS
DOCUMENT NUMBER: 137:261470
TITLE: Immunoregulatory properties of **mast**
cell-derived **exosomes**
AUTHOR(S): Dimitris, Skokos; Hany, Goubran-Botros; Michele, Roa;
Salah, Mecheri
CORPORATE SOURCE: Unite d'Immuno-allergie, Institut Pasteur, Paris,
75724, Fr.
SOURCE: Molecular Immunology (2002), 38(16-18), 1359-1362
CODEN: MOIMD5; ISSN: 0161-5890
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Transmission of information from **mast** cells to
neighboring or distant cells must be established continuously in order to
ensure homeostasis or to initiate immune and inflammatory responses.
Owing to their strategic location in peripheral tissues and their prompt
response to various stimuli, **mast** cells can be considered as the
cell prototype to fulfill such a sentinel function. There are several
ways for **mast** cells to communicate with other cells including
cell-cell interactions via membrane-assocd. receptors, cytokines and other
sol. mediators, and a newly described messenger which consists of membrane

vesicles called **exosomes** carrying a no. of immunoregulatory mols.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:95394 CAPLUS

TITLE: **Mast** cell-dependent B and T lymphocyte activation is mediated by the secretion of immunologically active **exosomes**

AUTHOR(S): Anon.

SOURCE: Journal of Immunology (2002), 168(3), 1496
CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal; Errata

LANGUAGE: English

AB Unavailable

L12 ANSWER 6 OF 10 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2002040582 EMBASE

TITLE: Erratum: **Mast** cell-dependent B and T lymphocytes activation is mediated by the secretion of immunologically active **exosomes** (The Journal of Immunology (2001) 166 (868-876)).

AUTHOR: Skokos D.; Le Panse S.; Villa I.; Rousselle J.-C.; Peronet R.; David B.; Namane A.; Mecheri S.

SOURCE: Journal of Immunology, (1 Feb 2002) 168/3 (1496).
ISSN: 0022-1767 CODEN: JOIMA3

COUNTRY: United States

DOCUMENT TYPE: Journal; Errata

FILE SEGMENT: 026 Immunology, Serology and Transplantation

LANGUAGE: English

L12 ANSWER 7 OF 10 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2002036162 EMBASE

TITLE: New insights into the immunoregulatory functions of mast cells.

AUTHOR: Mecheri S.

CORPORATE SOURCE: S. Mecheri, Immuno-allergy unit, Institut Pasteur, 28, rue du Docteur-Roux, 75015 Paris, France

SOURCE: Revue Francaise d'Allergologie et d'Immunologie Clinique, (2002) 42/1 (6-10).

Refs: 21

ISSN: 0335-7457 CODEN: RFAIBB

COUNTRY: France

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 026 Immunology, Serology and Transplantation

029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB **Mast** cells, which are preferentially located in connective tissues and epithelial layers, are now recognized as effector cells that participate in innate and acquired immunity. Upon activation with various secretagogues, **mast** cells release a large number of mediators stored in their secretory granules which consist of inflammatory mediators, cytokines, proteoglycans and neutral proteases. In addition to soluble mediators, **mast** cell granules have recently been shown to harbour small vesicles with immunoregulatory properties. Isolated **exosomes** have been shown to activate B and T lymphocytes and act as potent adjuvants for specific antibody responses in vivo. In this article I will discuss the mechanisms by which **mast** cells fulfill immunoregulatory functions that may be beneficial for the host. .COPYRGT. 2002 Editions scientifiques et medicales Elsevier SAS.

L12 ANSWER 8 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:151543 BIOSIS
DOCUMENT NUMBER: PREV200200151543
TITLE: New-found regulators of angiogenesis: Platelet- and tumor-cell-derived microparticles.
AUTHOR(S): Janowska-Wieczorek, Anna; Majka, Marcin (1); Kijowski, Jacek; Libura, Jola; Marquez, Leah; Zhao, Dongling; Ross, Lisa; Kawa, Milosz (1); Ratajczak, Mariusz Z. (1)
CORPORATE SOURCE: (1) James Graham Brown Cancer Center, Univ. of Louisville, Louisville, KY USA
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 2, pp. 54b.
<http://www.bloodjournal.org/>. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 2 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971.

DOCUMENT TYPE: Conference
LANGUAGE: English

AB Microparticles (MP) are circular membrane fragments shed from the surface of activated eukaryotic cells or secreted as **exosomes**. MP in the environment of the growing tumor may be derived from i) the tumor cells by shedding, ii) peripheral blood (PB) platelets activated by tumor cells and iii) tumor-infiltrating lymphocytes, monocytes and **basophils**. We hypothesize that MP are important but under-appreciated components of the microenvironment of growing tumors that may modulate their biology. In support of this we found that MP are secreted from many human tumor cell lines (neuroblastomas, rhabdomyosarcomas, lung cancer, melanomas), that their secretion is increased (up to 20 times) after exposure of these cells to chemokines (RANTES, MIP-1 α , etc.) and complement protein (C3a), and that these tumor cells may activate PB platelets which then release platelet-derived MP. To learn more about the biological effects of MP in tumorigenesis and angiogenesis we isolated and purified MP from tumor cells and activated PB platelets and subsequently exposed tumor and endothelial cells (HUVEC) to them. We observed that MP stimulated phosphorylation of MAPK p42/44, activated the PI-3K-AKT axis in several tumor cell lines and significantly increased the secretion of the angiogenic factors VEGF and FGF-2. Moreover, incubation of these cell lines with platelet-derived MP modified the activities of the matrix metalloproteinases (MMPs), necessary for endothelial cell migration and proliferation, that they secreted. We found after exposure to MP the active form of MMP-2 (which was inhibited by o-phenanthroline) in several neuroblastoma (6 out of 6 cell lines) and rhabdomyosarcoma (5/6) cell lines. Furthermore, MP derived from tumor cell lines chemo-attracted HUVEC directly and stimulated their proliferation in vitro. Generally, the biological effects of PMPs were only partly reduced by heat inactivation or trypsin digest, indicating that, in addition to the protein components of PMPs, lipid components are also responsible for their biological activity. Further studies are needed and are under way, however, to identify the PMP components that exert specific biological effects. We conclude that MP play an important role in angiogenesis by i) stimulating secretion of angiogenic factors by tumor cells, ii) activating MMP-2, and iii) stimulating endothelial cells directly. A better understanding of the role MP play in angiogenesis could help us to develop novel therapeutic anti-angiogenic approaches for treatment of various malignant disorders.

L12 ANSWER 9 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:199751 BIOSIS
DOCUMENT NUMBER: PREV200100199751
TITLE: Mouse and human mast cells secrete **exosomes** with immunostimulatory activity on B and T lymphocytes.
AUTHOR(S): Skokos, D. (1); Le Panse, S.; Villa, I. (1); Rousselle, J. C. (1); Peronet, R. (1); David, B. (1); Namane, A. (1); Mcheri, S. (1)
CORPORATE SOURCE: (1) Institut Pasteur, Paris France

SOURCE: Journal of Allergy and Clinical Immunology, (February, 2001) Vol. 107, No. 2, pp. S295. print.
Meeting Info.: 57th Annual Meeting of the American Academy of Allergy, Asthma and Immunology New Orleans, Louisiana, USA March 16-21, 2001
ISSN: 0091-6749.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L12 ANSWER 10 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:97843 BIOSIS
DOCUMENT NUMBER: PREV199799397046
TITLE: Release of MHC class II-enriched **exosomes** during **mast** cell degranulation.
AUTHOR(S): Bonnerot, C. (1); Raposo, G.; Mercheri, S.; Tenza, D.; Desaymard, C.
CORPORATE SOURCE: (1) Inst. Curie, Section Recherche, 25 rue Dr. Roux, 75015 Paris France
SOURCE: Molecular Biology of the Cell, (1996) Vol. 7, No. SUPPL., pp. 610A.
Meeting Info.: Annual Meeting of the 6th International Congress on Cell Biology and the 36th American Society for Cell Biology San Francisco, California, USA December 7-11, 1996
ISSN: 1059-1524.
DOCUMENT TYPE: Conference; Abstract; Conference
LANGUAGE: English

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FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 09:53:51 ON 11 DEC 2002
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L2 75 S L1 AND VESICLE?
L3 0 S L2 AND MASTOCYST?
L4 0 S L2 AND MASTOCYTE?
L5 0 S L1 AND MASTOCYTE
L6 38 S L2 AND EXOSOME?
L7 0 S L6 AND BASOPHIL?
L8 16 DUP REM L6 (22 DUPLICATES REMOVED)
L9 1291 S (BASOPHIL? OR MAST) (P) VESICLE
L10 22 S (BASOPHIL? OR MAST) (P) EXOSOME?
L11 12 DUP REM L10 (10 DUPLICATES REMOVED)
L12 10 S L11 NOT L6

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L2 75 S L1 AND VESICLE?
L3 0 S L2 AND MASTOCYST?
L4 0 S L2 AND MASTOCYTE?
L5 0 S L1 AND MASTOCYTE
L6 38 S L2 AND EXOSOME?
L7 0 S L6 AND BASOPHIL?
L8 16 DUP REM L6 (22 DUPLICATES REMOVED)
L9 1291 S (BASOPHIL? OR MAST) (P) VESICLE
L10 22 S (BASOPHIL? OR MAST) (P) EXOSOME?
L11 12 DUP REM L10 (10 DUPLICATES REMOVED)
L12 10 S L11 NOT L6

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